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Substitute for form 1449/PTO		Complete if Known	
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> <i>(Use as many sheets as necessary)</i>		Application Number	Not yet assigned 10/807,508
		Filing Date	Herewith
		First Named Inventor	Stanley M. Crain
		Art Unit	Not yet assigned 1614
		Examiner Name	Not yet assigned R. Henley
		Attorney Docket Number	96700/879
Sheet	1	of	1

## **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**

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Application Number	Not yet assigned 10/807,508
Filing Date	Herewith
First Named Inventor	Stanley M. Crain
Art Unit	Not yet assigned 1664
Examiner Name	Not yet assigned R. Henley
Attorney Docket Number	96700/879

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**U. S. PATENT DOCUMENTS**

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## **FOREIGN PATENT DOCUMENTS**

**Examiner  
Signature**

Date  
Considered

2/27/05

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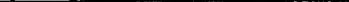
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Substitute for form 1449A/PTO				<b>Complete if Known</b>	
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> <i>(use as many sheets as necessary)</i>				Application Number	10/114,909 1U/807,508
				Filing Date	April 3, 2002
				First Named Inventor	Stanley M Crain
				Art Unit	1614
				Examiner Name	Raymond J. Henley III
Sheet	1	of	1	Attorney Docket Number	96700/748

U.S. PATENT DOCUMENTS

## FOREIGN PATENT DOCUMENTS

Examiner Initials	Cite No. <sup>1</sup>	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T
		Country Code <sup>3</sup> - Number <sup>4</sup> - Kind Code <sup>5</sup> (if known)				
<i>[Signature]</i>	3	EP 0 352 361 A1	01-31-1990	The Rockefeller University		

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## INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 1 of 3

### Complete if Known

Application Number	09/261,381 /0/807,508
Filing Date	March 3, 1999
First Named Inventor	Stanley M. Crain
Group Art Unit	1614
Examiner Name	Ray Henley
Attorney Docket Number	96700/453

### OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
	1	CHAMI, et al., Treatment of Constipation-Predominant Irritable Bowel Syndrome (IBS-C) with the Opioid Antagonist Naloxone Glucuronide (NG), The American Journal of Gastroenterology 1993, 88(9), 1568.	
	2	FARTHING, New Drugs in the Management of the Irritable Bowel Syndrome, Drugs 1998;56(1), 11-21.	
	3	DAPOIGNY, et al., Efficacy of Peripheral Kappa Agonist Fedotozine versus Placebo in Treatment of Irritable Bowel Syndrome, Digestive Diseases and Sciences 1995, 40(10) 2244-2248.	
	4	DROSSMAN, et al., Irritable Bowel Syndrome: A Technical Review for Practice Guideline Development, Gastroenterology 1997, 112:2120-2137.	
	5	DALTON, et al., Diagnosis and Treatment of Irritable Bowel Syndrome, American Family Physician 1997, 55(3):875-880.	
	6	CAMILLERI, et al., Review Article: Irritable Bowel Syndrome, Aliment. Pharmacol. Ther. 1997, 11:3-15.	
	7	PACE, et al., Therapy of Irritable Bowel Syndrome - An Overview, Digestion 1995, 56:433-442.	
	8	DELVAUX, et al., Trimebutine: Mechanism of Action, Effects on Gastrointestinal Function and Clinical Results, The Journal of International Medical Research 1997, 25:225-246.	
	9	DAPOIGNY, et al., Neurophysiology and Neuropsychiatry of the IBS, Digestion 1997, 58:1-9.	
	10	JUNIEN, et al., Review Article: The Hypersensitive Gut - Peripheral Kappa Agonists as a New Pharmacological Approach, Aliment. Pharmacol. Ther. 1995, 9:117-126.	
	11	GUE, et al., The K Agonist Fedotozine Modulates Colonic Distention - Induced Inhibition of Gastric Motility and Emptying in Dogs, Gastroenterology 1994, 107:1327-1334.	

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Substitute for form 1449B/PTO				Complete if Known	
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> <i>(use as many sheets as necessary)</i>				Application Number	09/264,361 /0/807,508
				Filing Date	March 3, 1999
				First Named Inventor	Stanley M. Crain
				Group Art Unit	1614
				Examiner Name	Ray Henley
Sheet	2	of	3	Attorney Docket Number	96700/453

OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS					
Examiner Initials'	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.			
	12	DROSSMAN, et al., <i>Psychosocial Factors in the Irritable Bowel Syndrome</i> , Gastroenterology 1988, 95:701-8.			T <sup>2</sup>
	13	DROSSMAN, et al., <i>U.S. Householder Survey of Functional Gastrointestinal Disorders</i> , Digestive Diseases and Sciences, 1993, 38(9):1569-1580.			
	14	TALLEY, et al., <i>Medical Costs in Community Subjects with Irritable Bowel Syndrome</i> , Gastroenterology 1995, 109:1736-1741.			
	15	KONIECZKO, et al., <i>Antagonism of Morphine-Induced Respiratory Depression with Naloxone</i> , Br. J. Anaesth. 1988, 61:318-323.			
	16	WANG, et al., <i>Morphine Tolerance and Physical Dependence: Reversal of Opioid Inhibition to Enhancement of Cyclic AMP Formation</i> , Journal of Neurochemistry 1995, 64(3):1102-1106.			
	17	JOSHI, et al., <i>Effects of prophylactic Naloxone on the Incidence of Morphine-related Side Effects in Patients Receiving Intravenous Patient-controlled Analgesia</i> , Anesthesiology 1999, 90:1007-11.			
	18	XU, et al., <i>Opioids Can Enhance and Inhibit the Electrically Evoked Release of Methionine-Enkephalin</i> , Brain Research 1989, 504:36-42.			
	19	GINTZLER, <i>Relevance of Opioid Bimodality to Tolerance/Dependence Formation</i> , Advances in Experimental Medicine and Biology, 373:73-83. (NO DATE AVAILABLE)			
	20	HORAN, et al., <i>Antinociceptive Profile of Biphalin, a Dimeric Enkephalin Analog</i> , The J. of Phar. and Exper. Ther. 265(3):1446-1454. (NO DATE AVAILABLE)			
	21	CHESKIN, et al., <i>Assessment of Naloxone Glucuronide as a Selective Gut Opioid Antagonist</i> , Drug and Alcohol Dependence 1995, 39:151-154.			
	22	GAN, et al., <i>Opioid-sparing Effects of a Low-dose Infusion of Naloxone in Patient-administered Morphine Sulfate</i> , Anesthesiology 1997, 87:1075-81.			

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## INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet

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### Complete if Known

Application Number	<b>09/261,361 10/18/97, 508</b>
Filing Date	<b>March 3, 1999</b>
First Named Inventor	<b>Stanley M. Crain</b>
Group Art Unit	<b>1614</b>
Examiner Name	<b>Ray Henley</b>
Attorney Docket Number	<b>96700/453</b>

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	23	<b>CRAIN, et al., Modulation of Opioid Analgesia, Tolerance and Dependence by Gs -coupled, GM1 Ganglioside-regulated Opioid receptor Functions, TIPS 1998, 19:358-365.</b>	
	24	<b>CRAIN, et al., GM1 Ganglioside-induced Modulation of Opioid Receptor-mediated Functions, Annals of the New York Academy of Sciences 1998:106-125.</b>	
	25	<b>APFEL, et al., Kappa Opioid Receptors Participate in Nerve Growth Factor-Induced Hyperalgesia, Neuroscience 1995, 68(4):1199-1206.</b>	
	26	<b>SHEN, et al., Nerve Growth Factor Rapidly Prolongs the Action Potential of Mature Sensory Ganglion Neurons in Culture, and This Effect Requires Activation of Gs-coupled Excitatory k-Opioid Receptors on These Cells, The Journal of Neuroscience 1994, 14(9):5570-5579.</b>	
	27	<b>SHEN, et al., Ultra-low Doses of Naltrexone or Etorphine Increase Morphine's Antinociceptive Potency and attenuate Tolerance/Dependence in Mice, Brain Research 1997, 757:176-190.</b>	
	28	<b>SHEN, et al., Biphalin, an Enkephalin Analgo with Unexpectedly High Antinociceptive Potency and Low Dependence Liability in Vivo, Selectively antagonized Excitatory Opioid Receptor Functions of Sensory Neurons in Culture, Brain Research 1995, 701:158-166.</b>	
	29	<b>SHEN, et al., Chronic Selective Activation of Excitatory Opioid Receptor Functions in Sensory Neurons Results In Opioid 'Dependence' Without Tolerance, Neuroscience 1992, 59:74-83.</b>	
	30	<b>CRAIN, After Chronic Opioid Exposure Sensory Neurons Become Supersensitive to the Excitatory Effects of Opioid Agonists and Antagonists as Occurs After Acute Elevation of GM1 Ganglioside, Brain Research 1992, 575:13-24.</b>	
	31	<b>CRAIN, et al., Opioids can Evoke Direct Receptor-Mediated Excitatory Effects on Sensory Neurons, Pharmacological Sciences 1990, 11(2):77-81.</b>	
	32	<b>CRAIN, et al., Ultra-low Concentrations of Naloxone Selectively Antagonize Excitatory Effects of Morphine on Sensory Neurons, Thereby Increasing its Antinociceptive Potency and Attenuating Tolerance/Dependence During Chronic Cotreatment, Proc. Natl. Acad. Sci. (USA) 1995, 92:10540-10544.</b>	
	33	<b>SHEN, et al., Dual Opioid Modulation of the Action Potential Duration of Mouse Dorsal Root Ganglion Neurons in Culture, Brain Research 1989, 491:227-242.</b>	

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